General

Guideline Title

ACR Appropriateness Criteria® pretreatment planning of invasive cancer of the cervix.

Bibliographic Source(s)

Siegel CL, Glanc P, Deshmukh SP, Dudiak KM, Gaffney DK, Green ED, Harisinghani MG, Henrichsen TL, Jolly S, Khati NJ, Kim YB, Lakhman Y, Moore DH, Nyberg DA, Pannu HK, Poder L, Rao GG, Simpson L, Javitt MC, Expert Panel on Womenâ€™s Imaging and Radiation Oncologyâ€“Gynecology. ACR Appropriateness CriteriaÂ® pretreatment planning of invasive cancer of the cervix. Reston (VA): American College of Radiology (ACR); 2015. 12 p. [69 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Siegel CL, Andreotti RF, Cardenes HR, Brown DL, Gaffney DK, Horowitz NS, Javitt MC, Lee SI, Mitchell DG, Moore DH, Rao GG, Royal HD, Small W Jr, Varia MA, Yashar CM, Expert Panel on Women's Imaging and Radiation Oncology-Gynecology. ACR Appropriateness Criteria® pretreatment planning of invasive cancer of the cervix. [online publication]. Reston (VA): American College of Radiology (ACR); 2011. 9 p. [67 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

ACR Appropriateness Criteria®

Clinical Condition: Pretreatment Planning of Invasive Cancer of the Cervix

Variant 1: FIGO stage Ib1, tumor size <4cm.

Radiologic Procedure	Rating	Comments	RRL*
MRI pelvis without and with contrast	8	DWI improves interobserver agreement and accuracy and helps distinguish post biopsy change. MRI and FDG-PET/CT are complementary examinations.	O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation
MRI pelvis without and with contrast	8	MRI and FDG-PET/CT are complementary	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation
CT chest, abdomen, and pelvis without and with contrast	8		O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation
FDG-PET/CT whole body	8	MRI and FDG-PET/CT are complementary	
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation

Radiologic Procedure	Rating	Comments	RRL*
		examinations.	
MRI pelvis without contrast	6		O
CT abdomen and pelvis with contrast	5		
X-ray chest	4		
CT abdomen and pelvis without contrast	2		
US abdomen	2		O
US pelvis transabdominal	2		O
US pelvis transvaginal	2		O
CT abdomen and pelvis without and with contrast	1		
X-ray contrast enema	1		
X-ray intravenous urography	1		
Tc-99m bone scan whole body	1		
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 2: FIGO stage Ib2, tumor size >4 cm.

Radiologic Procedure	Rating	Comments	RRL*
MRI pelvis without and with contrast	9	DWI improves interobserver agreement and accuracy and helps distinguish post biopsy change. MRI and FDG-PET/CT are complementary examinations.	O
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level
Tc-99m bone scan whole body	1	MRI and FDG-PET/CT are complementary examinations.	

Radiologic Procedure	Rating	Comments	RRL*
MRI pelvis without contrast	6		O
X-ray chest	5		
CT abdomen and pelvis with contrast	5		
CT abdomen and pelvis without contrast	2		
US pelvis transvaginal	2		O
US pelvis transabdominal	2		O
US abdomen	2		O
CT abdomen and pelvis without and with contrast	1		
X-ray contrast enema	1		
X-ray intravenous urography	1		
Tc-99m bone scan whole body	1		
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Variant 3: FIGO stage >Ib.

Radiologic Procedure	Rating	Comments	RRL*
MRI pelvis without and with contrast	9	DWI improves interobserver agreement and accuracy and helps distinguish post biopsy change. MRI and FDG-PET/CT are complementary examinations.	O
FDG-PET/CT whole body	9	MRI and FDG-PET/CT are complementary examinations.	
CT abdomen and pelvis with contrast	7		
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation

Radiologic Procedure	Rating	Comments	RRL*
CT chest with contrast	6		
MRI pelvis without contrast	6		O
CT chest without contrast	4		
CT abdomen and pelvis without contrast	2		
X-ray chest	2		
US pelvis transabdominal	2		O
US abdomen	2		O
TC-99m bone scan whole body	2	This procedure is used with stages >II or with symptoms of bone metastases.	
US pelvis transvaginal	2		O
CT abdomen and pelvis without and with contrast	1		
CT chest without and with contrast	1		
X-ray intravenous urography	1		
X-ray contrast enema	1		
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Note: Abbreviations used in the tables are listed at the end of the "Major Recommendations" field.

Summary of Literature Review

Introduction/Background

Cervical cancer is the third most common gynecological malignancy in the United States. It is estimated that during 2015 there will be approximately 12,900 new cases of cervical cancer and 4,100 deaths from this disease in the United States. The American Cancer Society reports that the death rate from cervical cancer decreased 29% from 1991 to 2003, but it did not significantly change from 2002 to 2012. This

improvement in mortality has been attributed to a significant increase in detection of early-stage, small cancers due to the development of the Papanicolaou smear. However, only minor improvement has been achieved in the survival rate for invasive cervical cancer. Established risk factors for cervical cancer include early sexual activity, especially with multiple partners, cigarette smoking, immunosuppression, and infection with human papilloma viruses 16 and 18 and other high-risk serotypes.

The prognosis of cervical carcinoma has been strongly linked to lymph node involvement by tumor. This, in turn, is predicted clinically and pathologically by the stage of disease, the volume of the primary tumor, and the histologic grade. The current official staging system for cervical cancer is based on the International Federation of Gynecology and Obstetrics (FIGO) classification. It defines the clinical staging system for cervical carcinoma based on clinical assessment, including physical examination under anesthesia, colposcopy, endocervical curettage, hysteroscopy, cystoscopy, proctoscopy, intravenous urography, barium enema (BE), and radiographs of lungs and skeleton. Although various imaging tests are selected, cross-sectional imaging with computed tomography (CT) or magnetic resonance imaging (MRI) is not essential. Errors in clinical FIGO staging have been consistently reported, with understaging of Ib-IIIb cancer varying from 20% to 40%. Overstaging of FIGO IIIb cancer in up to 64% of patients has also been reported.

Inaccuracy in clinical staging is predominantly due to difficulties in evaluating parametrial and pelvic sidewall invasion, bladder or rectal wall invasion, and metastatic spread; in evaluating primary endocervical (endophytic) tumors; and in estimating primary tumor size, especially the craniocaudal dimension. Aside from the inaccuracies of clinical staging, evaluation of lymph node metastasis, which is an important prognostic factor and a determinant in treatment planning, is not included in the clinical staging system. In spite of these limitations of clinical FIGO staging, modern cross-sectional imaging modalities such as ultrasound (US), CT, and MRI have not been incorporated into FIGO staging. Arguments against the use of CT or MRI as staging tools include their high cost and possible lack of availability, especially in the underdeveloped regions of the world where invasive cervical cancer is the most prevalent. Because of the limitations of clinical staging, cross-sectional imaging is frequently used in the United States. The results are used for treatment planning but are not included in reporting the FIGO stage.

Current Role of Imaging

The most important issue in treatment planning for cervical cancer is to distinguish early disease (stages Ia, Ib, and IIa) that can be treated with surgery from advanced disease that must be treated with radiation therapy or chemoradiation. In addition, for those with advanced disease, imaging is used to define the radiation therapy fields by delineating the anatomical extent of disease. Conventional radiological studies such as excretory urography, BE, and lymphangiography (LAG) are rarely, if ever, used today. There has been an increase in the use of cross-sectional imaging, particularly CT, MRI and positron emission tomography (PET)/CT.

Radiographs

Chest radiographs are obtained as a staging procedure to identify pleural effusion or pulmonary metastasis, which occur in the late stages of cervical cancer. However, chest CT is superior to radiographs in both cases.

Excretory Urography

Although excretory urography is a sensitive test for detecting urinary obstruction, CT, MRI and US reliably identify urinary tract obstruction. Excretory urography is not indicated in women with cervical cancer due to the limited information provided and ionizing radiation.

Ultrasound

Transabdominal US is a sensitive noninvasive means of detecting hydronephrosis but has a limited role in evaluating the local extent of the cervical cancer. Transrectal US (TRUS) and transvaginal US have been used in assessing local disease. The detection of parametrial disease and pelvic side wall involvement can be achieved with TRUS. The accuracies of TRUS and MRI were similar for tumor detection and parametrial infiltration. MRI has better soft-tissue contrast than US. TRUS is operator dependent and, due to the narrow field of view, gives no additional information on nodal status.

Computed Tomography

CT has staging accuracy ranging from 32% to 80% in cervical cancer. The sensitivity for parametrial invasion ranges from 17% to 100% with an average of 64%. There is a consensus in the literature that CT is most valuable in patients with advanced disease and that it has limited value (a positive predictive value of 58%) in evaluating early parametrial invasion. CT has been reported to have a high accuracy in depicting advanced disease. However, a recent ACRIN® trial reported that CT had sensitivity of only 42% for detecting advanced disease (>IIB), with sensitivity and specificity for detecting lymph node involvement of 31% and 86%, respectively.

The major limitation of CT in local staging is the inadequate differentiation between tumor and normal cervical stroma or parametrial structures. Therefore, CT is mainly used in advanced disease and in the assessment of lymph nodes. The positive predictive value of CT for nodal involvement

ranges from 51% to 65%, with negative predictive value ranging from 86% to 96%, and with sensitivities reported recently to range from 31% to 65%. CT detection of lymph node metastasis has a pooled sensitivity and specificity of 50% and 92%, respectively, on meta-analysis. The reliance on size criterion alone (>1 cm) for diagnosing malignant lymphadenopathy on CT is believed to account for the low sensitivity because micrometastases will be missed. CT shows distant metastases for radiotherapy planning and can be used to guide interventional procedures.

Magnetic Resonance Imaging

MRI is very accurate in determining tumor size, especially the craniocaudal extent, and tumor location (exophytic or endocervical). MRI is helpful in assessing the depth of stromal invasion to assess parametrial tumor extension and further local extension of the tumor. MRI is superior to clinical evaluation in assessing tumor size. MRI measurements are within 0.5 cm of the surgical size in 70% to 94% of cases. However, an ACRIN® trial reported that neither MRI nor CT was accurate for evaluating the cervical stroma. The use of endovaginal coils has been reported to be helpful in assessing small-volume disease. MRI after cone biopsy has significantly lower sensitivity and specificity for tumor detection.

The staging accuracy of MRI ranges from 75% to 96%. The sensitivity of MRI in evaluating parametrial invasion ranges from 40% to 57%, with a specificity of 77% to 80%. In studies that compare MRI and CT for evaluating parametrial invasion, MRI was superior to CT. Use of 3.0T MRI does not provide improvement in accuracy. The apparent diffusion coefficients (ADCs) calculated in cervical cancer are lower than those of normal cervical stroma, providing increased contrast between the normal cervical stroma and cervical tumor. The diffusion sequences require no intravenous contrast and add approximately 2 minutes to the MR protocol. The addition of diffusion-weighted imaging (DWI) improves interobserver agreement and is helpful, especially when the T2-weighted images are equivocal. In assessing local tumor invasion, T2-weighted and contrast-enhanced T1-weighted images are helpful. Small tumors may be better defined with postcontrast imaging. Lymph node metastases also show significantly decreased ADC values when compared to benign lymph nodes. Abnormal nodes as small as 5 mm may be detected with DWI. MR spectroscopy with choline measurements provides no additional benefit. In evaluating nodal disease, the sensitivity and specificity of MRI are 30% to 73% and 69% to 95%, respectively. These findings are similar to those of CT. Like CT, MRI also relies on size criteria for assessing lymph nodes and thus misses microscopic disease. The sensitivity of MRI in detecting lymph node metastases is reported to be both higher and lower than that of PET/CT in different studies. MRI had greater accuracy in detecting lymph node metastases in patients with tumors >4 cm in size.

Very few integrated PET/MRI scanners are in operation, and to date there have been no studies performed to detect or stage cervical cancer. The theoretical advantage of PET/MRI over PET/CT is the improved soft-tissue contrast, yielding better tissue characterization with MR. One study involved patients who had both a PET/CT examination and an MRI examination. The MR images were fused with the PET/CT images using a Windows workstation, and the alignment was verified in 3 planes. This study found an improved sensitivity with PET/MRI when compared to PET/CT (54% versus 44%, respectively) for metastic lymph node detection. No diffusion sequences were used in this protocol.

MRI can be a cost-effective staging technique. In a study of patients with Ib cervical cancer, those who underwent MRI as the initial imaging procedure for staging required fewer examinations and procedures compared with those who underwent tests such as BE, intravenous urogram, CT scan, cystogram, and proctoscopy. Tumor size >4 cm, cervical stromal invasion, and parametrial extension are correlated with increased risk of lymphadenopathy, which significantly affects patient management and prognosis for survival. Because these predictive criteria for the primary tumor are best evaluated radiologically, routine use of MRI has been recommended.

Lymphangiography and Lymphoscintigraphy

Lymphangiography (LAG) has technical limitations such as incomplete opacification of lymph node chains, occasional inability to cannulate one side, and lack of assessment of internal iliac nodes. For the pretreatment evaluation of lymph node metastases, LAG has been replaced by CT, MRI, and PET imaging. Preoperative lymphoscintigraphy can be used in patients undergoing sentinel node biopsy. Patients have Bleu Patente V injected in the cervix at the time of laparoscopy. The Bleu stained lymph nodes excised are correlated with lymph node radioactivity from a technetium (Tc)-99m cervical injection on the day of or day prior to laparoscopy. This is used to aid the surgeon in the operating room. High sensitivity (92%) and negative predictive value (98%) have been shown.

Positron Emission Tomography and Positron Emission Tomography/Computed Tomography

PET imaging is superior to CT and LAG in assessing pelvic and extrapelvic lymph nodes and organ involvement by cervical cancer. In the detection of metastatic lymph nodes in patients with cervical cancer, PET has been reported to have a sensitivity of 79% to 91% and a specificity of 95% to 100%. These values are higher than those for MRI and CT, although microscopic metastases may still be missed. Accuracy rates for lymph node metastases are reportedly higher for PET than MRI (78% versus 67%). Another study demonstrated that prognosis was best when patients had both PET-negative and CT-negative lymph node status and that the presence of PET-positive para-aortic lymph nodes was the most significant negative prognostic factor for progression-free survival. This same study found that PET using the tracer fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG) to assess lymph node status was the best predictor of overall survival in women with cervical cancer.

Hybrid PET/CT combines the functional metabolic imaging capabilities of PET with the spatial resolution of CT. Survival from cervical cancer can

be stratified based on the level of lymph node metastases detected on fluorodeoxyglucose-positron emission tomography (FDG-PET). Lymph node involvement in pelvic, para-aortic, and supraclavicular nodes is associated with increasingly poor prognosis. Recent studies report a sensitivity of 58% to 82%, specificity of 93% to 99%, and accuracy of 85% to 99% for PET/CT in detecting metastatic lymph nodes from cervical cancer. Another study showed that when abdominal CT is negative, PET has a sensitivity of 85.7%, a specificity of 94.4%, and an accuracy of 92% for detecting para-aortic lymph node metastasis in patients with advanced cervical cancer, prompting some to advocate routine PET imaging in such cases. In patients with early-stage cervical cancer (stages Ib–IIa, <4 cm), the value of FDG-PET for lymph node metastasis is decreased, with a sensitivity of 32%. A meta-analysis of imaging options found that FDG-PET/CT is the best predictor of lymph node status. The overall sensitivity of FDG-PET/CT is variable by stage and improves with higher-stage disease, likely because of the increased prevalence of lymph node–positive disease in higher-staged tumors. Lymph node status and maximum standardized uptake value (SUV_{max}) of the tumor were found to be the 2 top indicators of poor prognosis.

The tumor size, lymph node status, stage, and SUV_{max} are all important in predicting outcome. The SUV predicts metabolic activity and tumor proliferation and is associated with tumor size and lymph node metastases. High SUV_{max} with lymph node disease indicates a poor prognosis. Another study compared a low-SUV_{max} group of cervical cancer patients ($SUV_{max} = 9.6 \pm 2.6$) with a high-SUV_{max} group ($SUV_{max} = 19.9 \pm 4.9$). A higher rate of pelvic/para-aortic lymph node disease (73% versus 38%) was found in the high-SUV_{max} cohort. A group of authors found that a low SUV_{max} was associated with a better outcome in women treated with radiation therapy or concurrent chemotherapy. In addition to SUV_{max} tumor, standardized uptake value in pelvic lymph nodes (SUV_{PLN}) is an additional independent marker for prognosis. The SUV_{PLN} was not strongly correlated with SUV_{max} of the index tumor or to lymph node size but was predictive of patient survival. In addition to lymph node status, total lesion glycolysis (a volume-based parameter) may prove to be an additional independent predictor of prognosis.

FDG-PET/CT may alter cervical cancer treatment plans. In one study, 4 of 15 patients had significant changes of radiation therapy treatment plans after review of the FDG-PET/CT.

Nuclear Medicine Bone Scan

Bone scans do not seem warranted for initial screening in asymptomatic patients with stage 0, I, or II cervical carcinoma. Bone scintigraphy may be useful in patients with advanced disease (stage III and IV) who are symptomatic for bone metastases, such as with pain or hypercalcemia, and may not have access to PET/CT imaging. PET/CT did outperform CT and MRI in detecting hematogenous bone metastasis from cervical cancer. FDG-PET is more sensitive in detecting bone metastases in cancer patients than is bone scintigraphy.

Trachelectomy Assessment

Women with invasive cervical cancer stage Ia or small stage Ib who wish to retain fertility can be evaluated for trachelectomy, which is removal of the cervix, parametrial tissue, and cuff of the vagina. During the surgery a cerclage suture is placed across the uterine isthmus to maintain uterine competency in the event of a future pregnancy. Staging based on FIGO is not sufficient for these women, and precise identification of tumor extent up to, including, and beyond the internal os is essential. MRI will aid in assessment of patients wishing to preserve fertility, evaluating these inclusion criteria:

1. Tumor confined to the cervix, no tumor beyond the cervix or into the uterine body
2. No pelvic lymph node metastases
3. No evidence of impaired fertility
4. Tumor <2 mm (some centers will go up to 4 cm)

These women will require a careful evaluation to assess tumor size and the distance from the tumor to the internal os. One centimeter of preserved healthy cervical stroma is preferred; some surgeons will accept as little as 5 mm. Tumors ≤2 cm in size are associated with increased likelihood of trachelectomy surgery.

MRI is good at accurately measuring the distance of the tumor to the internal os. Nine of 9 patients with a ≤5-mm distance and 3 of 5 patients with a 6- to 9-mm distance required a radical hysterectomy because intraoperative assessment revealed a positive tumor resection margin. Unfortunately, small-volume cervical cancer tumor and post biopsy inflammatory changes may be indistinguishable on T2-weighted images. Recent studies of endovaginal MRI with DWI show promise. The DWI in conjunction with the T2-weighted images provided increased accuracy. Restricted diffusion was shown in the cervical cancer tumor and helped distinguish postbiopsy changes.

Tumor Stage Ib

Women with stage Ib1 who do not wish fertility preservation are also best evaluated with MRI as tumor visualization, tumor size accuracy and parametrial invasion are all best assessed on MRI when compared to CT. Nodal metastatic disease ranges from 10% to 30% in stage Ib1 disease,

depending on the tumor grade and volume and the presence or absence of lymph/vascular space invasion. It is essential to exclude lymph node metastatic disease in this group because curative surgery is not an option in the setting of lymph node metastatic disease. MRI had a sensitivity and specificity of 64% and 69%, respectively, for lymph node metastases in a cohort of 83 patients with FIGO stages Ib-II. FDG-PET/CT has a sensitivity ranging from 29% to 75% in early-stage cervical cancer. The specificity of FDG-PET/CT is high, ranging from 84% to 97%. The PET/CT sensitivity and specificity are 29% and 84%, respectively. MRI is more sensitive and FDG-PET is more specific. Overall accuracies are similar for the 2 tests: 65% and 68% for FDG-PET and MRI, respectively.

Patients with stage Ib2 tumors >4 cm are best evaluated with MRI because MRI assessment is better than CT assessment for tumor visualization, accuracy of tumor size, and parametrial invasion. FDG-PET/CT remains the best imaging test to assess lymph node metastases.

Tumor Stage >Ib

Tumors beyond stage Ib have spread beyond the confines of the cervix. Tumors spread to the upper vagina, stage IIa, can be surgically resected, whereas stage IIb tumors have invaded the parametrium and are treated not with surgery but rather with chemoradiation. These patients benefit from MRI evaluation of the index tumor for size and local invasion. FDG-PET/CT is beneficial in identifying metastatic disease and planning external radiation therapy.

Summary of Recommendations

- Imaging plays an essential role in pretreatment evaluation of women with invasive cervical cancer. It is used to assess tumor size and location; to detect involvement of the parametrium, pelvic sidewall and adjacent organs; and to search for lymph node metastases.
- MRI provides the best visualization of the primary tumor, estimation of tumor size and volume, and extent of soft tissue disease in the central pelvis.
- FDG-PET is the best modality in assessing nodal, extrapelvic and bone metastasis, and is also helpful in predicting patient outcome when SUV_{max} and SUV_{PLN} are incorporated into the assessment.
- Future studies may use the best of both techniques with MRI/PET fusion imaging.

Abbreviations

- CT, computed tomography
- DWI, diffusion-weighted imaging
- FDG-PET, fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography
- FIGO, International Federation of Gynecology and Obstetrics
- MRI, magnetic resonance imaging
- Tc, technetium
- US, ultrasound

Relative Radiation Level Designations

Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
O	0 mSv	0 mSv
	<0.1 mSv	<0.03 mSv
	0.1-1 mSv	0.03-0.3 mSv
	1-10 mSv	0.3-3 mSv
	10-30 mSv	3-10 mSv
	30-100 mSv	10-30 mSv
*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as "Varies."		

Clinical Algorithm(s)

Algorithms were not developed from criteria guidelines.

Scope

Disease/Condition(s)

Cervical carcinoma (invasive cancer of the cervix)

Guideline Category

Diagnosis

Evaluation

Clinical Specialty

Family Practice

Internal Medicine

Nuclear Medicine

Obstetrics and Gynecology

Oncology

Radiology

Intended Users

Advanced Practice Nurses

Health Plans

Hospitals

Managed Care Organizations

Physician Assistants

Physicians

Students

Utilization Management

Guideline Objective(s)

To evaluate the appropriateness of imaging modalities in the pretreatment evaluation of women with invasive cervical cancer

Target Population

Women with invasive cancer of the cervix

Interventions and Practices Considered

1. Magnetic resonance imaging (MRI), pelvis
    - Without and with contrast
    - Without contrast
2. Fluorodeoxyglucose-positron emission tomography (FDG-PET)/computed tomography (CT), whole body
3. CT
    - Abdomen and pelvis with contrast
    - Abdomen and pelvis without contrast
    - Abdomen and pelvis without and with contrast
    - Chest with contrast
    - Chest without contrast
    - Chest without and with contrast
4. X-ray
    - Chest
    - Contrast enema
    - Intravenous urography
5. Ultrasound (US)
    - Abdomen
    - Pelvis, transabdominal
    - Pelvis, transvaginal
6. Technetium (Tc)-99m bone scan, whole body

Major Outcomes Considered

- Utility of imaging modalities in the staging and pretreatment planning of cancer of the cervix
- Sensitivity, specificity, and staging accuracy of imaging modalities in the evaluation of cancer of the cervix

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Summary

Of the 67 citations in the original bibliography, 46 were retained in the final document. Articles were removed from the original bibliography if they were more than 10 years old and did not contribute to the evidence or they were no longer cited in the revised narrative text.

A new literature search was conducted in December 2013 to identify additional evidence published since the *ACR Appropriateness Criteria® Pretreatment Planning of Invasive Cancer of the Cervix* topic was finalized. Using the search strategy described in the literature search companion (see the "Availability of Companion Documents" field), 116 articles were found. Twelve articles were added to the bibliography. One hundred four articles were not used due to either poor study design, the articles were not relevant or generalizable to the topic, the results were unclear, misinterpreted, or biased, or the articles were already cited in the original bibliography.

The author added 11 citations from bibliographies, Web sites, or books that were not found in the new literature search.

See also the American College of Radiology (ACR) Appropriateness Criteria® literature search process document (see the "Availability of

Companion Documents" field) for further information.

Number of Source Documents

Of the 67 citations in the original bibliography, 46 were retained in the final document. The new literature search conducted in December 2013 identified 12 articles that were added to the bibliography. The author added 11 citations from bibliographies, Web sites, or books that were not found in the new literature search.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Definitions of Study Quality Categories

Category 1 - The study is well-designed and accounts for common biases.

Category 2 - The study is moderately well-designed and accounts for most common biases.

Category 3 - The study has important study design limitations.

Category 4 - The study or source is not useful as primary evidence. The article may not be a clinical study, the study design is invalid, or conclusions are based on expert consensus.

The study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);

Or

The study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;

Or

The study is an expert opinion or consensus document.

Category M - Meta-analysis studies are not rated for study quality using the study element method because the method is designed to evaluate individual studies only. An "M" for the study quality will indicate that the study quality has not been evaluated for the meta-analysis study.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

The topic author assesses the literature then drafts or revises the narrative summarizing the evidence found in the literature. American College of Radiology (ACR) staff drafts an evidence table based on the analysis of the selected literature. These tables rate the study quality for each article included in the narrative.

The expert panel reviews the narrative, evidence table and the supporting literature for each of the topic-variant combinations and assigns an appropriateness rating for each procedure listed in the variant table(s). Each individual panel member assigns a rating based on his/her interpretation of the available evidence.

More information about the evidence table development process can be found in the ACR Appropriateness Criteria® Evidence Table

Development document (see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

Rating Appropriateness

The American College of Radiology (ACR) Appropriateness Criteria (AC) methodology is based on the RAND/UCLA Appropriateness Method. The appropriateness ratings for each of the procedures or treatments included in the AC topics are determined using a modified Delphi method. An initial survey is conducted to elicit each panelist's expert interpretation of the evidence, based on the available data, regarding the appropriateness of an imaging or therapeutic procedure for a specific clinical scenario. The expert panel members review the evidence presented and assess the risks or harms of doing the procedure balanced with the benefits of performing the procedure. The direct or indirect costs of a procedure are not considered as a risk or harm when determining appropriateness (additional assumptions regarding rating appropriateness can be found in the document Rating Round Information). When the evidence for a specific topic and variant is uncertain or incomplete, expert opinion may supplement the available evidence or may be the sole source for assessing the appropriateness.

The appropriateness is represented on an ordinal scale that uses integers from 1 to 9 grouped into three categories: 1, 2, or 3 are in the category "usually not appropriate" where the harms of doing the procedure outweigh the benefits; and 7, 8, or 9 are in the category "usually appropriate" where the benefits of doing a procedure outweigh the harms or risks. The middle category, designated "may be appropriate," is represented by 4, 5, or 6 on the scale. The middle category is when the risks and benefits are equivocal or unclear, the dispersion of the individual ratings from the group median rating is too large (i.e., disagreement), the evidence is contradictory or unclear, or there are special circumstances or subpopulations which could influence the risks or benefits that are embedded in the variant.

The ratings assigned by each panel member are presented in a table displaying the frequency distribution of the ratings without identifying which members provided any particular rating. To determine the panel's recommendation, the rating category that contains the median group rating without disagreement is selected. This may be determined after either the first or second rating round. If there is disagreement after the first rating round, a conference call is scheduled to discuss the evidence and, if needed, clarify the variant or procedure description. If there is still disagreement after the second rating round, the recommendation is "may be appropriate."

This modified Delphi method enables each panelist to articulate his or her individual interpretations of the evidence or expert opinion without excessive influence from fellow panelists in a simple, standardized, and economical process. For additional information on the ratings process see the Rating Round Information document.

Additional methodology documents, including a more detailed explanation of the complete topic development process and all ACR AC topics can be found on the ACR Web site (see also the "Availability of Companion Documents" field).

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Magnetic resonance imaging (MRI) can be a cost-effective staging technique. In a study of patients with Ib cervical cancer, those who underwent MRI as the initial imaging procedure for staging required fewer examinations and procedures compared with those who underwent tests such as barium enema (BE), intravenous urogram, computed tomography (CT) scan, cystogram, and proctoscopy.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria (AC).

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The recommendations are based on analysis of the current medical evidence literature and the application of the RAND/UCLA appropriateness method and expert panel consensus.

Summary of Evidence

Of the 69 references cited in the *ACR Appropriateness Criteria® Pretreatment Planning of Invasive Cancer of the Cervix* document, 63 are categorized as diagnostic references including 1 well designed study, 21 good quality studies, and 24 quality studies that may have design limitations. Additionally, 4 references are categorized as therapeutic references including 1 good quality study. There are 20 references that may not be useful as primary evidence. There are 2 references that are meta-analysis studies.

While there are references that report on studies with design limitations, 23 well designed or good quality studies provide good evidence.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Imaging plays an essential role in pretreatment evaluation of women with invasive cervical cancer. It is used to assess tumor size and location; to detect involvement of the parametrium, pelvic sidewall and adjacent organs; and to search for lymph node metastases.

Potential Harms

Relative Radiation Level

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults. Additional information regarding radiation dose assessment for imaging examinations can be found in the ACR Appropriateness Criteria® Radiation Dose Assessment Introduction document (see the "Availability of Companion Documents" field).

Qualifying Statements

Qualifying Statements

- The American College of Radiology (ACR) Committee on Appropriateness Criteria (AC) and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists, and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate

other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the U.S. Food and Drug Administration (FDA) have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.

- ACR seeks and encourages collaboration with other organizations on the development of the ACR AC through society representation on expert panels. Participation by representatives from collaborating societies on the expert panel does not necessarily imply individual or society endorsement of the final document.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Siegel CL, Glanc P, Deshmukh SP, Dudiak KM, Gaffney DK, Green ED, Harisinghani MG, Henrichsen TL, Jolly S, Khati NJ, Kim YB, Lakhman Y, Moore DH, Nyberg DA, Pannu HK, Poder L, Rao GG, Simpson L, Javitt MC, Expert Panel on Womenâ€™s Imaging and Radiation Oncologyâ€“Gynecology. ACR Appropriateness CriteriaÂ® pretreatment planning of invasive cancer of the cervix. Reston (VA): American College of Radiology (ACR); 2015. 12 p. [69 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2015

Guideline Developer(s)

American College of Radiology - Medical Specialty Society

Source(s) of Funding

The American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

Guideline Committee

Committee on Appropriateness Criteria, Expert Panel on Women's Imaging and Radiation Oncology-Gynecology

Composition of Group That Authored the Guideline

Panel Members: Cary Lynn Siegel, MD (*Principal Author*); Phyllis Glanc, MD (*Panel Vice-chair*); Sandeep Prakash Deshmukh, MD; Kika M. Dudiak, MD; David K. Gaffney, MD, PhD; Edward D. Green, MD; Mukesh G. Harisinghani, MD; Tara Lynn Henrichsen, MD; Shruti Jolly, MD; Nadia J. Khati, MD; Young Bae Kim, MD; Yulia Lakhman, MD; David H. Moore, MD; David A. Nyberg, MD; Harpreet K. Pannu, MD; Liina Poder, MD; Gautam G. Rao, MD; Lynn Simpson, MD; Marcia C. Javitt, MD (*Specialty Chair*)

Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Siegel CL, Andreotti RF, Cardenes HR, Brown DL, Gaffney DK, Horowitz NS, Javitt MC, Lee SI, Mitchell DG, Moore DH, Rao GG, Royal HD, Small W Jr, Varia MA, Yashar CM, Expert Panel on Women's Imaging and Radiation Oncology-Gynecology. ACR Appropriateness Criteria® pretreatment planning of invasive cancer of the cervix. [online publication]. Reston (VA): American College of Radiology (ACR); 2011. 9 p. [67 references]

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the American College of Radiology (ACR) Web site .

Availability of Companion Documents

The following are available:

ACR Appropriateness Criteria®. Overview. Reston (VA): American College of Radiology; 2015 Oct. 3 p. Available from the American College of Radiology (ACR) Web site .

ACR Appropriateness Criteria®. Literature search process. Reston (VA): American College of Radiology; 2015 Feb. 1 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Evidence table development. Reston (VA): American College of Radiology; 2015 Nov. 5 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Topic development process. Reston (VA): American College of Radiology; 2015 Nov. 2 p. Available from the ACR Web site .

ACR Appropriateness Criteria®. Rating round information. Reston (VA): American College of Radiology; 2015 Apr. 5 p. Available from

the ACR Web site .
ACR Appropriateness Criteria®. Radiation dose assessment introduction. Reston (VA): American College of Radiology; 2015 Sep. 3 p. Available from the ACR Web site .
ACR Appropriateness Criteria®. Procedure information. Reston (VA): American College of Radiology; 2015 Jul; 2 p. Available from the ACR Web site .
ACR Appropriateness Criteria®. Manual on contrast media. Reston (VA): American College of Radiology; 2015; 129 p. Available from the ACR Web site .
ACR Appropriateness Criteria® pretreatment planning of invasive cancer of the cervix. Evidence table. Reston (VA): American College of Radiology; 2015. 32 p. Available from the ACR Web site .
ACR Appropriateness Criteria® pretreatment planning of invasive cancer of the cervix. Literature search. Reston (VA): American College of Radiology; 2015. 1 p. Available from the ACR Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on December 28, 2000. The information was verified by the guideline developer on January 25, 2001. This summary was updated by ECRI on February 1, 2006. This summary was updated by ECRI Institute on August 11, 2009. This summary was updated by ECRI Institute on January 13, 2011 following the U.S. Food and Drug Administration (FDA) advisory on gadolinium-based contrast agents. This summary was updated by ECRI Institute on March 20, 2012. This summary was updated by ECRI Institute on February 12, 2016.

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